National Marrow Donor Program®

Entrusted to operate the
C.W. Bill Young
Cell Transplantation Program

National Coordinating Center
3001 Broadway St. N.E.
Suite 100
Minneapolis, MN 55413-1753

Toll Free: 1 (800) 526-7809
Phone: (612) 627-5800
marrow.org

November 17, 2008

Commander Russell Shilling, USN
Program Officer, Medical Services Corps
Office of Naval Research (ONR 341)
875 N. Randolph St.
Arlington, VA 22203

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-06-1-0704 between the Office of Naval Research and the National Marrow Donor Program

Dear Commander Shilling:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of July 1, 2008 to September 30, 2008.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

C: D. Ivery – ACO (ONR-Chicago), letter and enclosure
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret): letter and enclosure
Jennifer Ng, PhD – C.W. Bill Young Marrow Donor Recruitment and Research Program, letter and enclosure
J. Rike - DTIC (Ste 0944): letter and enclosure
NRL (Code 5227): letter and enclosure
Dennis Confer, MD, Chief Medical Officer, NMDP, letter only
Michelle Setterholm, NMDP letter only

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
17-11-2008	Quarterly	Jul – Sep 2008

4. TITLE AND SUBTITLE
Quarterly Performance / Technical Report

5a. CONTRACT NUMBER
N/A

5b. GRANT NUMBER
N00014-06-1-0704

5c. PROGRAM ELEMENT NUMBER
N/A

6. AUTHOR(S)
Setterholm, Michelle

5d. PROJECT NUMBER
N/A

5e. TASK NUMBER
Project 1, 2, 3, 4

5f. WORK UNIT NUMBER
N/A

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
National Marrow Donor Program
3001 Broadway St., N.E., Ste. 500
Minneapolis, MN 55413

8. PERFORMING ORGANIZATION REPORT NUMBER
N/A

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Office of Naval Research
875 N. Randolph St.
Arlington, VA 22203

10. SPONSOR/MONITOR'S ACRONYM(S)
ONR

11. SPONSORING/MONITORING AGENCY REPORT NUMBER
N/A

12. DISTRIBUTION AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES
N/A

14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE	Same as Report	22	Dennis L. Confer, MD – Chief Medical Office
U	U	U			19b. TELEPONE NUMBER (*Include area code)* 612.362.3425

NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-06-1-0704

QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
JULY 01, 2008 to SEPTEMBER 30, 2008

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2008 through September 30, 2008

TABLE OF CONTENTS

IIA. Contingency Preparedness – Hypothesis 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1.1 Aim 1: Secure Interest of Transplant Physicians	**The NMDP works to educate physicians and their medical staff as well as to disseminate information about its contingency planning through this AIM.** **Period 8 Activity:** • During this period 323 Basic Radiation Training (BRT) exams were submitted by RITN centers; as of September 30, 2008 a total of 1,146 BRT exams had been submitted with a passing rate exceeding 95%. • During this period we initiated planning for a 2009 advanced training course for RITN centers to send staff to. The course is titled Advanced Radiation Medical Emergency training and will be conducted in Oakridge, TN at the Radiation Emergency Assistance Center/Training Site (REAC/TS). Class will be held on March 26 & 27. Course lessons included: o Basic Health Physics & Radiation Protection: Part I o A History of Serious Radiological Incidents: The Real Risk o Health Physics & Contamination Control: Part II o Radiation Detection, Monitoring & Protection Laboratory Exercise & Quiz o Diagnosis & Management of the Acute Radiation Syndrome (ARS) o Diagnosis & Management of Internal Contamination o Diagnosis & Management of Acute Local Radiation Injury & Case Review: Yanango Peru o Radiation Sources & Radiological Terrorism o Radiation Emergency Area Protocol Demonstration o Radiation Emergency Medical Management Drill o Radiation Dose Estimations – Problem Solving Session

IIA.1.2 Aim 2: GCSF in Radiation Exposure	**This AIM focuses on non-transplant treatment guidelines and patient assessment related to the use of GCSF for patient treatment as a result of radiation exposure.** **Period 8 Activity:** • During this period the analysis of RITN centers stockpiling GCSF in preparation for a radiological incident was completed and a memo summarizing the finding was distributed to RITN centers and select partners. o Project purpose: To determine the feasibility and effectiveness of a Radiation Injury Treatment Network (RITN) hospital managed increase in inventory of G-CSF. o Project scope: Limit evaluation to how increasing the inventory of G-CSF or a like product would affect RITN centers. If determined to be feasible the team will create a questionnaire for all RITN transplant centers to further investigate. o Project Findings 1) It is cost prohibitive to increase the inventory, to an effective level, maintained at RITN centers without full subsidization. 2) Further exploration is needed to validate the benefit of being able to treat an additional 1,739 victims, if a funding source if identified. 3) Further exploration of this topic should include the evaluation of peg-filgrastim. 4) Centers should follow existing SOPs regarding dosage determination (rounding to closest vial size vs. strict mcg/kg dosing). 5) Stockage levels of G-CSF should be increased regionally across the United States: 1. Addition to CDC Chempaks (Note: no refrigeration included in ChemPak). 2. Approach wholesalers to increase average stock level. 6) RITN should explore possibility with the CDC to purchase end of life G-CSF from SNS stockpile at a significant discount. This could also be a means to inexpensively increase stock levels at RITN centers, once on-hand inventory is increased there would be no significant additional cost to maintain.

IIA.1 3 Aim 3: Patient Assessment Guidelines and System Enhancements	**This AIM focuses on transplant treatment guidelines; including the refinement of guidelines for patient assessment, product selection and transplant in radiation exposure situations.** **Period 8 Activity:** • No activity this period
IIA 1.4 Aim 4: National Data Collection Model	**The focus of this AIM is to define and develop a national data collection and management model to collect data from a mass radiological exposure event.** **Period 8 Activity:** • Attended a meeting with the EBMT Nuclear Accident Committee Ulm, Germany from June 30 to July 1st, 2008. A portion of the meeting agenda was to discuss collaboration with European counterparts to standardize the data collection plan used in response to a radioactive disaster with mass casualties resulting in marrow toxic injuries. • Attendees included: o Judith Bader — United States Department of Health and Human Services, Washington, D.C. o Axel Böttger, MD — Germany Federal Ministry of Environment, Nature Protection and nuclear Safety, Bonn o Cullen Case — United States National Marrow Donor Program, Minneapolis, Minnesota o Nelson Chao, MD — United States Duke University, Radiation Countermeasures Center of Research Excellence, Durham, North Carolina o John Chute, MD — United States Duke University, Durham, North Carolina

	o Norman Coleman, MD Department of Health and Human Services, Washington, D.C.	United States
	o Dennis Confer, MD National Marrow Donor Program, Minneapolis, Minnesota	United States
	o Theodor M. Fliedner, MD Radiation Medicine Research Group, Ulm University	Germany
	o Arnold Ganser, MD Department of Hematology and Oncology, Medical University Hanover	Germany
	o Patrick Gourmelon, MD Institut de radioprotection et de sûreté nucléaire, Fontenay-aux-Roses	France
	o Dieter Graessle, Dipl.- Math. Oec. Radiation Medicine Research Group, Ulm University	Germany
	o Juergen Griebel, MD Institute of Radiation Hygiene, Federal Office for Radiation Protection, Munich	Germany
	o Robert Krawisz American Society for Blood and Marrow Transplantation, Arlington Heights, Illinois	United States
	o Viktor Meineke, MD Bundeswehr Institute of Radiology, Munich	Germany
	o Dietger Niederwieser, MD European Group for Blood and Marrow Transplantation and Department of Hematology and oncology, University of Leipzig	Germany
	o Matthias Port, MD Department of Hematology and Oncology, Medical University Hanover	Germany

	o Ray Powles, MD — United Kingdom Nuclear Accident Committee of EBMT, London o Bhawna Sirohi, MD — United Kingdom Nuclear Accident Committee of EBMT, London o David Weinstock, MD — United States Dana-Farber Cancer Institute, Boston Massachusetts o Albert Wiley, MD — United States Radiation Emergency Assistance Center/Training Site, Oak Ridge, Tennessee o Collette Steinwachs — Germany Radiation Medicine Research Group, Ulm University • As a result of this meeting a paper is being published to disseminate the points that European and US experts agreed upon.
IIA. Contingency Preparedness – Hypothesis 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
IIA.2.1 Aim 1: Contingency Response Network	**Efforts related to this AIM are focused on the development of the Radiation Injury Treatment Network (RITN), a permanent organization of transplant centers, donor centers and cord blood banks to maintain a contingency response network.** **Period 8 Activity:** • RITN task tracking: 27% of RITN centers have completed all of the tasks required for the agreement period (through October 31, 2008) as of September 30, 2008. • Exercises: o During this period through RITN's partnership with the World Health Organization - Radiation Emergency Medical Preparedness and Assistance Network (WHO-REMPAN) RITN participated in the International Atomic Energy Agency (IAEA) international nuclear emergency exercise ConvEx(3)2008. This exercise involved the response to an accidental release of ionizing radiation from a nuclear power plant in Mexico.

	○ During this period the NMDP conducted two functional exercises with NMDP staff. This allowed primary and back-up staff to each respond to a scenario that impacts NMDP operations at a significant level. ○ RITN centers continued to conduct self directed tabletop exercises based on the scenario provided to them by the NMDP and submit answers to key questions via the Internet once complete. • Meetings: Held three (3) conference calls with RITN centers to assist in completion of required tasks and to improve integration into the network. • Presented "Radiation Injury Treatment Network®: Hematology Physicians Preparing for a Mass Casualty Marrow Toxic Incident" at the Indo-US Workshop on Medical Countermeasures for Radiation Injury: Current and Evolving Technologies held from 17 – 20 August, 2008 in New Delhi, India. • RITN centers were identified as an asset to be called upon during both the Democratic National Convention in Denver, CO and the Republican National Convention in St. Paul, MN. ○ Local as well as regional centers were identified to respond to an incident. • Assistant Secretary of Preparedness and Response (DHHS) was provided with 24 hour contact information for the RITN Control Team in Minneapolis as well as contacts at each RITN center.
IIA.2.2 Aim 2: Sibling Typing Standard Operating Procedures	**This goal of this AIM is to develop and test standard operating procedures, in conjunction with core transplant centers, to manage the activities required to HLA type siblings of casualties to evaluate their potential as HSC donors for their affected family member.** **Period 8 Activity:** • No activity this period.

IIA. Contingency Preparedness – Hypothesis 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3.1 Aim 1: I.T. Disaster Recovery	**The focus of this AIM is to ensure NMDP's ability to access and utilize its information management and communication infrastructure in a contingency situation in which its Minneapolis Coordinating Center is damaged or destroyed.** **Period 8 Activity:** • **Business Continuity Planning:** o Emergency communications: ▪ During July 2008 we conducted an NMDP Network communication test, satellite telephone test, GETS card test, emergency notification system test, and a public announcement system test. ▪ Satellite telephone connectivity issues continue to cause problems at all RITN center locations. Global Star (satellite phone service provider) states that many satellites are aging and being deactivated and that they will be replaced in the future. With-in the emergency communication sector hopes are not high that Global Star will be able to accomplish this with the economy in the current state it is in. o Completed the development of the Business Impact Analysis (BIA) with key NMDP operational departments, identifying critical areas that would have high impact to operations if rendered inoperable. o Conducted business continuity site visits to two (2) NMDP operated donor centers. Distributed Business Continuity Action Guides, reviewed procedures in place, and discussed methods to improve preparedness at each location. o Continued to develop a business continuity plan incorporating a Critical Staff Recovery Site (CSRS) with no initial cost to the organization

IIB. Rapid Identification of Matched Donors – Hypothesis 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1.1 Aim 1: Increase Registry Diversity	**Period 8 Activity:** Six contracted HLA testing laboratories performed HLA-A, B, DRB1 typing on 44,089 newly recruited donors • Blind quality control testing error rate was 0.03%, meeting the project requirement of ≤ 1.5%. • On-time testing completion rate was 98%, meeting the project requirement of a minimum of 85% of typing results reported within 14 days of shipment of samples. • New agreements for the six laboratories were granted. The agreement period is September 29, 2008 to September 27, 2009. The weekly target for shipment of new donor samples has increased to 6401 samples. One laboratory will report HLA-A, B, **C**, and DRB1 for all of their samples typed each week. This laboratory receives 33% of the total samples sent each week for recruitment typing. • The NMDP will continue to focus on educating and motivating racial and ethnic minorities about the opportunity to save lives by joining the Registry and becoming a potential adult marrow donor for a patient in need. In support of this effort, we develop and produce a complete line of educational materials targeting multicultural communities. These materials are used by our adult donor recruitment teams to engage sponsors and potential Registry members in supporting our mission. Materials produced during this period included educational sell sheets targeting African American and Hispanic emergency responders. To increase Registry Diversity, a new line of materials was developed to increase awareness and education among expectant parents to encourage donation of their baby's umbilical cord blood to a public cord blood bank. • By providing educational brochures, awareness posters, recipient stories for the potential donors, and motivational posters to thank the OB/GYN hospital staff, the cord blood banks are able to extend their reach to more potential donors, particularly those of racial and ethnic diversity. • The materials are provided to the Network cord blood banks to increase quality conversations with eligible donors. Feedback from Network cord blood banks indicates overwhelming acceptance and high use of the new materials. Banks that have not previously used NMDP materials are now

	adopting the materials, and those who have ordered in the past are now ordering significant quantities, reflecting the value provided to the banks.
IIB.1.2 Aim 2: Evaluate HLA-DRB1 High Res typing	**Period 8 Activity:** This task is closed.
IIB.1.3 Aim 3: Evaluate HLA-C Typing of Donors	**Period 8 Activity:** This task is closed.
IIB.1.4 Aim 4: Evaluate Buccal Swabs	**Period 8 Activity:** The Sample Storage Research Study (SSRS) began in September, 2007. The first time point for donor swab evaluation was September, 2007. The donor samples for the second time point were sent in September, 2008. Results are pending. The first time point for Quality Control (QC) swab evaluation was December, 2007, and the second time point was June, 2008. • HLA results from the second time point were 100% accurate, at both the intermediate and high resolution levels. • All samples amplified well from the primary DNA extraction. The DNA analysis showed a decrease in the average 260/280 ratios from 2.6 to 1.9. A ratio of 1.8 to 2.0 is considered good. • 1.2Kb C locus amplicon of each sample was visualized on an agarose gel. The amplicons were comparable between the first and second time points with clear and crisp bands indicating high quality DNA.
IIB 1.5 Aim 5: Enhancing HLA Data for Selected Donors	**Period 8 Activity:** This aim consists of two prospective, registry-based typing projects, which have the potential to strategically identify and improve the HLA typing and availability of donors most likely to match searching patients from domestic TCs. The primary goal of the Replacement Donor Pilot Study was to identify an HLA-A, B, DRB1 identical

	replacement donor for every donor selected for workup by a TC. • NMDP staff continued to monitor the patient-directed utilization of donors typed in this project. The primary objective of the Optimum Donor Pilot Study was to develop a systematic strategy to classify adult donors into phenotype categories based upon the likelihood to appear on a patient's search. Adult donors with high potential to match searching patients were selected and proactively contacted to verify availability, upgrade HLA, and/or secure additional stored samples in an effort to increase the utilization of NMDP donors and to help reduce the search times for patients. • NMDP staff continued to ship approximately 700 donor samples for prospective HLA typing. Donor selection strategies were extended to include pilot strategies for the search for potentially matching HLA-A, B only typed donors for patient phenotypes without a potential 6 of 6 HLA match in the NMDP Registry. • NMDP staff continued to monitor the patient-directed utilization of donors typed through the project.
IIB. Rapid Identification of Matched Donors – Hypothesis 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB 2.1 Aim 1: Collection of Primary Data	**Period 8 Activity:** • No activity this period.
IIB 2.2 Aim 2: Validation of Logic of Primary Data	**Period 8 Activity:** • This task is closed.
IIB 2.3 Aim 3: Reinterpretation of Primary Data	**Period 8 Activity:** • This task is closed.
IIB 2.4 Aim 4: Genotype Lists & Matching Algorithm	**Period 8 Activity:** • No activity this period.

IIB. Rapid Identification of Matched Donors – Hypothesis 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3.1 Aim 1: Phase I of EM Haplotype Logic	**Period 8 Activity:** • No activity this period.
IIB 3.2 Aim 2: Enhancement of EM Algorithm	**Period 8 Activity:** • No activity this period.
IIB 3.3 Aim 3: Optimal Registry Size Analysis	**Period 8 Activity:** • No activity this period.
IIB 3.4 Aim 4: Target Under-represented Phenotypes	**Period 8 Activity:** • No activity this period.
IIB 3.5 Aim 5: Bioinformatics Web Site	**Period 8 Activity:** • No activity this period.
IIB 3.6 Aim 6: Consultants to Improve Algorithm	**Period 8 Activity:** • Funding on this Aim supports the Search Strategy Advice (SSA) program provided to TCs to support their need for expert HLA expertise. The program includes external and internal HLA experts who review each patient search and write a report summarizing a search strategy; both internal and external experts participate in a rigorous QC program. This report assists the TC in rapidly identifying the best potential stem cell source for their patient. The SSA program completed 379 patient reports for 67 TCs during this quarter. The average turnaround time for all reviews was 3.5 business days which exceeded our program requirement of 5 business days. Through their consistent high use of the matching algorithm and associated tools, the HLA Experts were able to flag several patient cases where further investigation of the algorithm may provide

	improved search results.
IIB. Rapid Identification of Matched Donors – Hypothesis 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4.1 Aim 1: Expand Network Communications	**Period 8 Activity:** • No activity this period.
IIB.4.2 Aim 2: Central Contingency Management	**Period 8 Activity:** • We completed the second in a series of continuing medical education (CME) seminars for physicians who refer for transplantation. This goal of this program was to continue to educate on the role and timing of transplantation for Myelodysplastic Sydrome (MDS), and the proper application of the therapy vs. other choices, particularly in older adults. The program is offered as a live Web/audio conference, on CD-ROM, and also online in our Physicians' Resource Center for a period of one year. This allows clinicians to access the program when they are available and increases attendance. This program was a part of an extensive educational effort toward referring physicians, to increase their education on the advances in transplant survival, the importance of referral timing, and the expanding patient eligibility, in order to prepare them for referral for transplantation.
IIC. Immunogenetic Studies – Hypothesis 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1.1 Aim 1: Donor Recipient Pair Project	**Period 8 Activity:** In 1994 a retrospective Donor/Recipient Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. • The review and resolution of outstanding typing results continued for Sample Group (SG) 19 with completion and data audit anticipated in the next quarter.

	• The period of performance for SG20 came to a close on August 31, 2008. SG20 consisted of 410 donor/recipient pairs and 90 cord/recipient pairs. Data review is in process. • The contracts for SG21 (500 pairs) testing were awarded to four labs. SG21 contracts will include intermediate and high resolution HLA and also presence/absence testing for 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1). • The project period for SG21 began September 1, 2008 and continues until December 31, 2008.
IIC. Immunogenetic Studies – Hypothesis 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC 2.1 Aim 1: Analysis of non-HLA loci	**Period 8 Activity:** In 2005 a pilot study to perform high resolution KIR gene typing was launched. The primary objectives of the study were to move technology forward from the current practice of locus level typing to high resolution typing, disseminate information and protocols in an open source mechanism and develop reference lines for use in individual laboratories. • The final 91 KIR discrepancies were resolved via a tiebreaker lab. • Resolution of new alleles found within Phase 1, 2 and 3 of the KIR Typing Pilot project continues. • Clinical correlation of KIR alleles with HSCT outcome proceeded within the International Histocompatibility Working Group – HCT component. Preliminary results presented at the 15th IHIWS suggest that high expression variants of KIR 3DL1 alleles carried by the donor may influence relapse rates in HSCT for myeloid disease. Further analysis will be completed during the next quarter. • The IPR database application will allow for storage and analysis of all immunogenetic data collected on NMDP research samples. This database will replace the existing HLA donor/recipient pairs database and facilitate storage and analysis of data from other immunogenetic loci (KIR, microsatellites, single nucleotide polymorphisms, etc.).

IIC 2.2 Aim 2: Related Pairs Research Repository	**Period 8 Activity:** Related transplant research sample collection continued with a pilot project initiated at seven TCs in December 2007. At the end of the current quarter, 266 samples (119 donor/recipient pairs) had been submitted to the Repository. A programmer continues to develop the Research Sample Repository Tools suite to facilitate management of samples. Enhancements to the tools will be tested and released to production next quarter.
IID. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1.1 Aim 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 8 Activity:** The Cord Blood Research sub-Committee met monthly to discuss study priorities and plan analyses. Activity during the past quarter focused on the following areas: • Planned several Cord Blood related sessions for the upcoming NMDP Council meeting o A workshop entitled, "CFU Methodologies: Considerations in Practice Standards and Outcome Variability", that will cover issues related to the current CFU assay systems and new procedures designed to minimize interlab variability. o A workshop entitled, “New Frontiers in Cord Blood Processing”, that will provide an overview of cord blood processing methodologies and systems. o A wet lab for cord blood bank technicians focused on best practices for CFU assay setup and enumeration. • Initiated two pilot projects: o A study was initiated to evaluate differential cellular recoveries for CBUs from various race groups with a focus on determining root causes of low cell yields from African American CBUs observed by several committee members. Data collection is in process at several committee members laboratories with data analysis expected to begin in the next quarter. o The cell processing laboratory at Memorial Sloan-Kettering recently developed a modified gating strategy for CD34 viability assessment that correlates with engraftment potential in a single center study. The committee is evaluating the gating strategy in a retrospective review of CD34 viability at several member laboratories. Data analysis will begin next quarter.

Observational Research

- Staff continued work on various observational studies within the area of Immunobiology and GVHD.
- A total of 6 abstracts were submitted to 2009 ASH meetings of which all were accepted. Three for poster and 3 for oral presentations.
- A total of two manuscripts from the GVHD Working Committee were submitted to journals during this reporting period. One manuscript was accepted during this period.

Prospective Studies; RCI BMT

- Activity related to the BMT CTN PBSC vs. Marrow trial continued with a total of 455 donor/patient pairs randomized at the end of this reporting quarter. Accrual at the end of September was 83% complete. We continue to see an increase in work-ups and randomizations which directly reflects efforts made to increase accrual and the goal of completion in early 2009.
- Adult Double Cord trial activity during this period included the activation of an additional sites for a total of 8 sites open to accrual. Two patients were enrolled during this quarter for a total of 7 patients which meets our expected accrual goals. Staff coordinated and completed monthly PI and coordinator calls.
- Revlemid trial activity continued to progress forward. During this reporting period initial database design and review occurred. At the end of September staff were in the process of completing database testing. It is expected that site training and opening to accrual will occur in the next reporting period.
- Activity continued on protocol development for the AZA study titled *Low Intensity Therapy of MDS Prior to Non-Ablative Allogeneic Stem Cell Transplantation.* Additional funding is being explored to support portions of this study.

Staff continued to work to close the Renal Cell Carcinoma trial. All sites completed the required data entry into the study database. Study was officially closed with NMDP IRB. Final Study closure and monitoring is in progress including database closure activities.

IID.1.2 Aim 2: Research with NMDP Donors	**Period 8 Activity:** • Staff continued support of a Donor Ethnicity study with Dr. Galen Switzer from the University of Pittsburgh. • Staff continued to collaborate on a COG KIR study. Activities include facilitating the collection of a donor blood sample and shipment to the study lab. To date, four requests have been facilitated. • Staff continued to assess options for centralizing the NMDP long-term donor follow-up. A cross-functional team of NMDP staff was formed to draft a protocol. Established a timeline for implementation of a pilot to assess the centralization. • Staff working out logistical details for obtaining donor samples to support study assessing use of allogeneic cytotoxic T-lymphocytes in children with acute leukemia.
IID.1.3 Aim 3: Expand Immuno-biology Research	**Period 8 Activity:** The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies • Six abstracts were submitted and accepted for presentation at the 2008 American Society of Hematology meeting: o Woolfrey A, Klein J, Haagenson M, Spellman S, Petersdorf E, Oudshoorn M, Gajewski J, Hale G, Horan J, Battiwalla M, Marino S, Setterholm M, Kollman C and Lee SJ. **Evaluation of Human Leukocyte Antigen (HLA) Matching Requirements for Unrelated Peripheral Blood Stem Cell (PBSC) Transplantation.** Accepted for oral presentation. o Bojesen SE, Malkki M, Gooley T, Zhao LP, Selvakumar A, Spellman S, Petersdorf E, Hansen JA and Dupont B. **Genetic allelic variation in the p53 DNA repair pathway constitute a risk factor for long-term survival in hematopoietic stem cell transplantation.** Accepted for oral presentation. o Marino S, Lin S, Maiers M, Haagenson M, Spellman S, Lee SJ, Wang T, Klein J and van Besien K. **Identifying amino acid substitution positions associated with day 100 survival in unrelated donor stem cell transplant using Random Forest analysis**. Accepted for poster presentation. o Valcárcel D, Kan F, Wang T, Lee SJ, Spellman S, Hale G, Marino S, Marks D, McCarthy P, Oudshoorn M, Petersdorf E, Ringdén O, Setterholm M, Sierra J. **One antigen HLA-mismatch**

related and 8/8 allele matched unrelated donors are associated with similar survival after hematopoietic cell transplantation for acute leukemia. Accepted for poster presentation.

- Nguyen Y, Al-Lehibi A, Gorbe E, Li E, Haagenson M, Wang T, Spellman S, Lee SJ and Davidson NO. **Insufficient evidence for association of NOD2/CARD15 or other inflammatory bowel disease-associated markers with GVHD or other outcomes in T-replete, unrelated donor transplantation facilitated by the NMDP.** Accepted for poster presentation.
- Fernandez-Vina M, Klein J, Haagenson M, Spellman S, Lee SJ, Anasetti C, Baxter-Lowe L, Cano P, Flomenberg N, Horowitz M, Hurley C, Oudshoorn M, Petersdorf E, Setterholm M, Champlin R and de Lima M. **The clinical significance of matching for alleles at the low expression HLA loci DP, DQ and DRB3/4/5 in unrelated hematopoietic stem cell transplantation.** Accepted for oral presentation.

- IBWC staff focused efforts on studies targeted for submission for presentation at the 2009 BMT Tandem Meetings. Abstracts are due early in the next quarter.
- The IBWC co-scientific director participated in the IHWG Hematopoietic Cell Transplant Component of the 15th International Histocompatibility and Immunogenetics Workshop (IHIWS). The IBWC also sponsored an exhibition booth during the IHIWS conference to facilitate outreach to basic scientists and international investigators.

Funding for CIBMTR IBWC studies:

- Research funds were awarded to support the distribution of research samples for a study investigating development of a prognostic score for unrelated donor HSCT for CML.
- Research funds supported development of a prospective research sample collection protocol for a study of cGVHD in long term surviving male recipients who received HSCT from female donors. Potential study subjects received mailings to solicit participation in the project during the quarter. Prospective collection of blood samples from consented study participants will begin next quarter.

ACRONYM LIST

AABB	American Association of Blood Banks	IND	Investigational New Drug
AML	Acute Myelogenous Leukemia	ICRHER	International Consortium for Research on Health Effects of Radiation
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IS	Information Services
ASBMT	American Society for Blood and Marrow Transplantation	IT	Information Technology
ASHI	American Society for Histocompatibility and Immunogenetics	IRB	Institutional Review Board
B-LCLs	B-Lymphoblastoid Cell Lines	KIR	Killer Immunoglobulin-like Receptor
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	NCI	National Cancer Institute
BRT	Basic Radiation Training	MHC	Major Histocompatibility Complex
C&A	Certification and Accreditation	MICA	MHC Class I-Like Molecule, Chain A
CBMTG	Canadian Blood and Marrow Transplant Group	MICB	MHC Class I-Like Molecule, Chain B
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NCBM	National Conference of Black Mayors
CBS	Canadian Blood Service	NIH	National Institutes of Health
CBU	Cord Blood Unit	NIMS	National Incident Management System
CHTC	Certified Hematopoeitic Transplant Coordinator	NK	Natural Killer
CIBMTR	Center for International Blood & Marrow Transplant Research	NMDP	National Marrow Donor Program
CLIA	Clinical Laboratory Improvement Amendment	NRP	National Response Plan
CME	Continuing Medical Education	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
COG	Children's Oncology Group	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CREG	Cross Reactive Groups	OIT	Office of Information Technology
CT	Confirmatory Testing	OMB	Office of Management and Budget
CTA	Clinical Trial Application	ONR	Office of Naval Research

CTAC	Clinical Trial Application Committee	PBMC	Peripheral Blood Mononuclear Cells
DIY	Do it yourself	PBSC	Peripheral Blood Stem Cell
DKMS	Deutsche Knochenmarkspenderdatei	PCR	Polymerase Chain Reaction
DMSO	Dimethylsulphoxide	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
D/R	Donor/Recipient	RCC	Renal Cell Carcinoma
EBMT	European Group for Blood and Marrow Transplantation	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
EM	Expectation Maximization	REAC/TS	Radiation Emergency Assistance Center/Training Site
EMDIS	European Marrow Donor Information System	RFP	Request for Proposal
FBI	Federal Bureau of Investigation	RFQ	Request for Quotation
FDA	Food and Drug Administration	RITN	Radiation Injury Treatment Network
Fst	Fixation Index	SBT	Sequence Based Typing
GETS	Government Emergency Telecommunications Service	SCTOD	Stem Cell Therapeutics Outcome Database
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SG	Sample Group
GvHD	Graft vs Host Disease	SSP	Sequence Specific Primers
HHS	Health and Human Services	SSOP	Sequence Specific Oligonucleotide Probes
HIPAA	Health Insurance Portability and Accountability Act	STAR®	Search, Tracking and Registry
HLA	Human Leukocyte Antigen	TC	Transplant Center
HML	Histoimmunogenetics Mark-up Language	TED	Transplant Essential Data
HR	High Resolution	TNC	Total Nucleated Cell
HRSA	Health Resources and Services Administration	TSA	Transportation Security Agency
HSC	Hematopoietic Stem Cell	URD	Unrelated Donor
IBWC	Immunobiology Working Committee	WMDA	World Marrow Donor Association
IDM	Infectious Disease Markers	WU	Work-up
IHWG	International Histocompatibility Working Group		